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10/551,482	07/31/2006	Wynne Weston-Davies	2488-1-011	4162

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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,482	WESTON-DAVIES, WYNNE	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 11-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Currently amended claims 1, 3, 11, 15 (11/4/09) and previously presented claims 2-5, 12-14 are pending and under consideration by the Examiner.

2. Receipt of Applicant's arguments and amendments filed on 11/4/2009 is acknowledged.

3. The following previous rejections and objections are withdrawn in light of applicants amendments filed on 11/4/09:

(i) the rejection of claims 1-5, 11-15, under 35 U.S.C. 112, second paragraph.

Applicant's arguments with respect to claims 1-5, 11-15, have been considered but are moot in view of the new ground(s) of rejection over claims 1-5.

4. Applicant's arguments filed on 11/4/2009 have been fully considered but were persuasive in part. The issues remaining and new issues are stated below.

Claim rejections-35 USC § 112, first paragraph, scope of enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 1-5, 11-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a bronchoconstrictive disease, ARDS, by administering EV131 protein comprising the amino acid sequence set forth in SEQ ID NO:6, does not reasonably provide enablement for a method as recited in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is maintained for reasons of record set forth at pages 3-11 of the previous Office action (6/1/2009).

Applicants argue that with regard to the issues raised in connection with the treatment of bronchoconstrictive diseases, the inventor was the first person to demonstrate that the removal of histamine from a disease site using EV131 counteracts neutrophil-mediated diseases, the effect of histamine depletion on neutrophil-mediated diseases had not been identified prior to the disclosure of the present invention, previous attempts to explore the influence of histamine on neutrophil-mediated diseases suggested only a marginal effect of histamine on diseases within this category and as described in the specification at page 2, lines 22-32, the failure of these previous studies to appreciate the significant role of histamine in neutrophil-mediated diseases was likely due to the experimental design of these earlier studies, which targeted histamine receptors rather than histamine. Applicants also argue that given that the present inventor has demonstrated for the first time a pivotal role of histamine in neutrophil-mediated diseases, an ordinarily skilled practitioner would appreciate that other neutrophil-mediated diseases would benefit from treatment using EV131 to remove histamine from relevant disease sites, such a practitioner would realize, based on his/her experience, which neutrophil-mediated diseases would be most likely to respond to EV 131, what the relevant sites involved in such diseases are, and how to administer EV 131 thereto. Furthermore, Applicants argue that additional details pertaining to pharmaceutical compositions and administration thereof are presented in the specification at page 7, line 6 through to page 9, line 3, a number of documents published after the priority date of the present application show that EV131 positively influences allergic asthma and adult respiratory distress syndrome (ARDS), and exemplary of such documents, a paper by

Couillin et al. (2004, J. Immunol. 173:3281-3286) and an abstract by Couillin et al. (2005, Ann. NY Acad. Sci. 1056:197-205) are submitted herewith for the Examiner's consideration. However, contrary to Applicants arguments, Applicants have misconstrued the rejection by the Examiner. The instant claims are drawn very broadly to methods of treating all bronchoconstrictive diseases ranging from ARDS to cystic fibrosis. However, other than the inhibition of bronchoconstrictive disease induced by endotoxin by administering EV131 of amino acid sequence set forth in SEQ ID NO:6, the specification fails to provide any guidance for the successful treatment of all the disparate bronchoconstrictive diseases. Applicants have failed to show the nexus between administration of EV131 and treatment of cystic fibrosis, which encompasses alleviation of the symptoms of cystic fibrosis. In the instant case, a method of treating cystic fibrosis, is very different from a method of treating ARDS. Furthermore, the limited results presented for bronchoconstriction induced by endotoxin, are not sufficient to enable the breadth of the claims and are not predictive of in vivo efficacy for treatment of all bronchoconstrictive conditions. Given the breadth of claim 1 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of skill in the art to practice the claimed invention.

Claim rejections-35 U.S.C. 112, second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected as vague and indefinite for several reasons.

Claim 1, lines 7-8, recites the limitation "the sequence motif". There is insufficient antecedent basis for this limitation in the claim.

Claim 1, line 9, recites the limitation "the sequence motif". There is insufficient antecedent basis for this limitation in the claim.

Claim 1, lines 7-10, are vague and indefinite because they recite the new limitation "…wherein the fragment comprises the sequence motif aspartic acid (D)/glutamic acid (E), alanine (A), tryptophan (W), and lysine (K)/arginine (R) and the sequence motif tyrosine (Y)/cysteine (C), glutamic acid/aspartic acid (D), leucine (L)/isoleucine (I)/phennylalanine (F) and tryptophan (W)." It is unclear from this recitation whether the amino acids are a contiguous sequence. It is suggested that the claim be amended to recite the sequence motif as recited in the specification and for which there is a proper basis.

Claims 2-5, are rejected as vague and indefinite insofar as they depend on the above rejected claim 1 for their limitations.

Claim rejections-35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7a. Claims 1-2, 4-5, 11-14, are rejected under 35 U.S.C. § 102(b) as being anticipated by WO 99/271104.

This rejection is maintained for reasons of record set forth at pages 12-13 of the previous Office action (6/1/2009).

Applicants argue that the reference WO 99/27104 only discloses the use of EV131 as an anti-inflammatory agent or as an agent useful for counteracting the effects of allergic reactions and that this reference fails to mention neutrophil-mediated diseases and, furthermore, fails to teach or recite treatment of neutrophil-mediated diseases with antihistamine agents. However, contrary to Applicants arguments, bronchoconstrictive disease is an allergic reaction involving neutrophil migration and chemotaxis, and anti-inflammatory agents are administered in the treatment of the disease. The EV131 protein of the prior art would have the same effect as the instant claims when administered. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp.*

v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) Once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the Examiner presents evidence or reasoning to show inherency, the burden shifts to the Applicant to show the difference.

Furthermore, it would be expected that the EV131 protein once administered, would have the same effect in the treatment of bronchoconstrictive disease. Once a reference teaching a product appearing to be substantially identical is made the basis of a rejection, and the Examiner presents evidence or reasoning to show inherency, the burden shifts to the Applicant to show the difference.

"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

With respect to the instant claims, the instantly claimed method would be an inherent property of the prior art method because in both methods EV131 protein is being administered. Newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent. See MPEP. 2112-2112.02. See *Bristol-Myers Squibb Company v. Ben Venue Laboratories* 58 USPQ2d 1508 (CAFC 2001) in which the Court found

that preamble language in claims of patents directed to administration of anticancer drug are expressions of purposes and intended results, and as such are non-limiting, since language does not result in manipulative difference in steps of claims. It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

While the prior disclosure is silent as to the treatment of ARDS (the elected species) by administration of EV131 protein, the instant claims merely recite a newly discovered result, i.e. treatment of ARDS, a known method to the same use of EV131 protein as recited in claims 3 and 15, which are not being rejected under 35 USC 102(b). The claimed process is not directed to a new use, it is the same use and it consists of the same method as described by the reference.

Therefore, the method disclosed in reference meets the limitations recited in claims 1-2, 4-5, and 11-14.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject

matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8a. Claims 1-5, 11-15, are rejected under 35 U.S.C. § 103 as being unpatentable over WO 99/27104 A .

This rejection is maintained for reasons of record set forth at pages 13-15 of the previous Office action (6/1/2009).

Applicants argue that WO 99/27104 fails to mention neutrophil-mediated diseases, fails to mention ARDS, infant respiratory distress syndrome (IRDS), severe acute respiratory syndrome (SARS), chronic obstructive airways disease (COPD), cystic fibrosis, and ventilator induced lung injury (VILI) as recited in claims 3 and 15 and therefore WO 99/27104 fails to render obvious the present claims. However, contrary to Applicants arguments, if the reference recited the specific diseases, this rejection would be a 35 USC 102(b) rejection rather than a 35

USC 103 rejection and all pending claims 1-5 and 11-15 would have been rejected under 35 USC 102(b). Therefore, the method disclosed in reference renders obvious claims 1-5, and 11-15.

Conclusion

Claims 1-5, and 11-15, are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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